Summer 2016
Vol. 21 No. 3

LabLink

this issue

Director, Bureau of Laboratories, Sandip Shah, Ph.D., HCLD(ABB)

Bureau Vision:
The Bureau of Laboratories is a stronger, more diverse team within an integrated public health system. We utilize advanced technology and innovative leadership to provide comprehensive public health services in our dynamic global community.

Bureau Mission:
We are dedicated to continuing leadership in providing quality laboratory science for healthier people and communities through partnerships, communication and technical innovation.

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MDHHS
Michigan Department of Health & Human Services
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Zika Virus Testing at MDHHS Bureau of Laboratories

Author: Janice Matthews-Greer, PhD, DABMM, Section Manager, Virology and Immunology

In response to the emergence of Zika virus, the MDHHS laboratory is now able to provide testing. Since Zika, Dengue, and Chikungunya viruses show similar clinical presentations in patients and are spread by the same mosquito genus in the same geographic region, testing for Dengue and Chikungunya is performed when Zika virus testing is requested.

Preapproval is required before submission of specimens for testing. Accurate dates for both illness onset and travel to Zika-endemic areas are required. Call your local health department or MDHHS epidemiologists at 517-335-8165 for approval.

Specimen Collection and Submission

Diagnostic testing for Zika virus can be accomplished using molecular and serologic methods available at the BOL. Serum tests include, the **CDC Trioplex Real-Time RT-PCR** (polymerase chain reaction) assay for viral nucleic acid, the CDC **IgM capture MAC-ELISA** assay for Zika antibodies, and an InBios **IgM capture ELISA** for Dengue and Chikungunya IgM antibodies. Urine, cerebrospinal fluid (CSF), and amniotic fluid specimens will be accepted for Zika PCR testing **ONLY** if they are accompanied by serum specimens.

- Specimen collection and submission guidelines may be found here.
- IgM serology (ELISA) test information may be found here.
- PCR test information may be found here.

All specimens must be accompanied by a test requisition and a supplemental questionnaire. Please use the **new (DCH-0583) form** found at: www.michigan.gov/documents/DCH-0583TEST_REQUEST_7587_7.pdf

The questionnaire can be found at: www.michigan.gov/documents/mdhhs/MichiganZikaSupplementalQuestionnaire_5-5-2016_003_524044_7.pdf

Testing Algorithm:

Specimen source and test selection are dependent on the time period from specimen collection and the onset of symptoms.

Date of specimen collection is within **3 days of symptom onset.**	Date of specimen collection is **4-7 days of symptom onset.**	Date of specimen collection is **7-14 days after symptom onset.**	Date of specimen collection is **2-12 weeks after symptom onset.**
Test Requested	**Test Requested**	**Test Requested**	**Test Requested**
• Zika PCR (serum and urine) • Dengue PCR (serum) • Chikungunya PCR (serum)	• Zika PCR (serum and urine) • Zika IgM (serum) • Dengue PCR & IgM (serum) • Chikungunya PCR & IgM (serum)	• Zika PCR (urine) • Zika IgM (serum) • Dengue IgM (serum) • Chikungunya IgM (serum)	• Zika IgM (serum) • Dengue IgM (serum) • Chikungunya IgM (serum)

Notes:

PCR (above) refers to real-time Reverse Transcriptase (RT)-PCR, a test for RNA. The BOL utilizes the Trioplex RT-PCR under an Emergency Use Authorization (EUA) for Zika virus testing of urine and serum. The test is a multiplex assay for three RNA viruses; Zika, Dengue, and Chikungunya. Note that Zika viremia may be prolonged in pregnant women, but 7 days is considered the cutoff for obtaining a positive serum PCR.

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(Zika continued from page 2)

False negative results are likely to occur after that time. The time interval in which the urine is most likely to test PCR positive is between 3 and 14 days. Positive PCR results are considered final and may not be followed by a confirmatory test.

Zika virus IgM antibody capture enzyme-linked immunosorbent assay (ELISA) is EUA-authorized for testing serum and cerebrospinal (CSF) fluid. However, if CSF is submitted for Zika IgM detection, a paired serum sample collected at the same time must be included. Note that Dengue and Chikungunya IgM testing cannot be performed on CSF. Positive or equivocal serology results are normally confirmed by Plaque Reduction Neutralization Assay (PRNT) before reporting the result. Negative results are considered final.

CDC Interim Guidance issued on May 13, 2016, recommends Zika virus PCR testing of urine collected less than 14 days after symptoms onset, in conjunction with a patient serum to be tested using the appropriate molecular or serologic assay, based on the number of days since post-symptom onset.

Results

Specimens with positive or equivocal results for Zika, Dengue, or Chikungunya virus IgM will be forwarded to the CDC for confirmation. In addition, PRNT will be performed to delineate between true Zika IgM and cross-reactivity with other flaviviruses, (e.g. Yellow Fever, Dengue), as well as non-specific reactions found in health conditions such as pregnancy or Malaria. All positive and equivocal serology results should be considered **PRESUMPTIVE** until further PRNT testing is performed. Normally, in a primary response to virus infection, detectable levels of IgM are temporary and more likely to be non-specific early in the immune response, whereas neutralizing antibodies include those of the IgG class which are long-lasting. Unfortunately, these flaviviruses are so closely-related antigenically that Zika virus-specific neutralizing antibody can be difficult to discriminate, even by PRNT. In such cases, the final result may be reported as positive for a recent flavivirus infection, instead of for Dengue or Zika infection.

It is important for the laboratory to know if the patient has been vaccinated with either the Japanese Encephalitis or Yellow Fever vaccine, as this is likely to result in cross-reactive, and even high-titered antibodies to Zika virus. Chikungunya does not cross-react with flaviviruses because it is an alphavirus, but positive results are sent for confirmation due to the similarity of disease symptoms, the existence of a common endemic region, and the need to ensure Zika virus infection is ruled out.

CDC fact sheet link for health care providers, patients and pregnant women may be found at: www.cdc.gov/zika/state-labs/index.html#FDA-fact

For more information on Zika virus or Zika virus testing please refer to the Michigan Emerging Disease Issues website at: www.michigan.gov/emergingdiseases
or the CDC Zika information site at: www.cdc.gov/zika/
To receive important public health updates and emergency information on Zika virus and other laboratory topics, subscribe to the MiHAN by emailing your request to Carrie Anglewicz, anglewiczc@michigan.gov.

How to Navigate the Website for Laboratory Information

Start at **Michigan.gov**; click **DHHS** in the' Popular:' line; click **Doing Business with MDHHS**; go to **Health Care Providers**, then **Lab Services**. [Bookmark or Save this as a Favorite in your browser.] Zika Virus Testing and other emerging issues may be found under the **What's New?** section of the Lab Services page. In addition, an A-Z Test Listing link provides the comprehensive list of tests performed at the BOL. Click on each test to view specimen collection and submission guidelines.

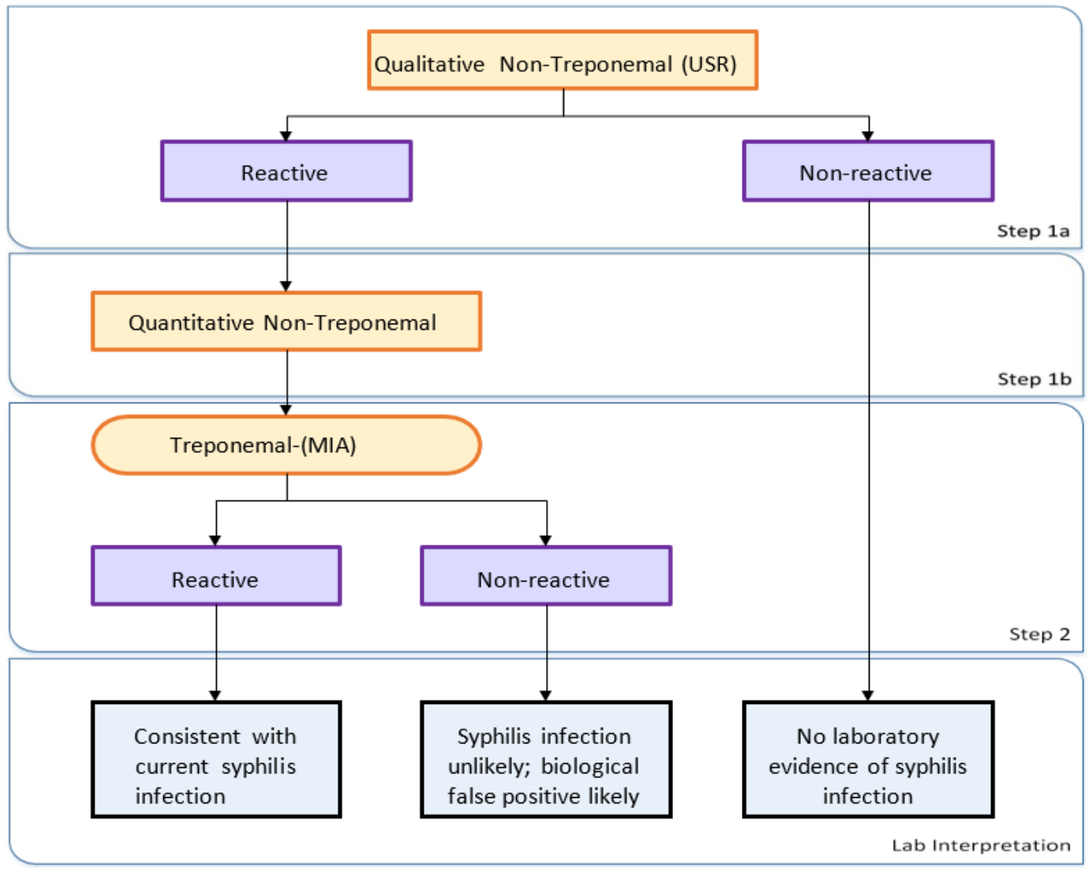
MDHHS Bureau of Laboratories to Change Syphilis Algorithm

Author: Kristine Smith, MT (ASCP), Unit Manager of Bacterial and Viral Serology

The Michigan Department of Health & Human Services Bureau of Laboratories will be changing methodology for syphilis treponemal antibody testing beginning on July 5, 2016. We will continue to follow the forward syphilis algorithm as recommended by the CDC (see chart below), but instead of the *Treponema pallidum* Particle Agglutination (TP-PA) assay for the detection of treponemal antibodies, confirmatory testing will be performed using the Multiflow ImmunoAssay (MIA) on the Bio-Rad BioPlex® 2200 instrument. The validation studies at BOL showed a 95.3% accuracy rate when comparing the BioPlex® 2200 with the current TP-PA method, and other studies have also shown comparable sensitivity/specificity rates between both assays.

TP-PA methodology is based on the agglutination of patient (IgM/IgG) antibody with gelatin particles sensitized with *Treponema pallidum* (Nichols strain) antigen. The new technology relies on the simultaneous detection of IgG antibodies bound to beads coated with three recombinant antigens associated with *T. pallidum* (15kDa, 17kDa and 47 kDa). Studies have shown that for specific *T. pallidum* antibodies, the time difference for detection of IgG antibodies compared to IgM is negligible (generally within just a few days). If clinically indicated, a second specimen collected 2-4 weeks later may be submitted for re-testing. The required specimen source will remain as serum.

As of July 5, 2016, if the TP-PA box is checked on our current test requisition, the MIA will be performed in its place. However, the TP-PA will continue to be offered when MIA results are either equivocal, uninterpretable, or by prior authorization only. We will discontinue the use of the Fluorescent Treponemal Antibody (FTA) assay, as this test is no longer recommended by the CDC as a confirmatory method due to its low specificity.



Syphilis IgG Multiplex ImmunoAssay (MIA) results will be reported as follows:

Result	Interpretations for Syphilis IgG MIA
REACTIVE	Treponemal antibodies are present.
EQUIVOCAL	Equivocal results are obtained when the sample index is just below the positive assay cutoff value. See TP-PA results.
NONREACTIVE	Treponemal antibodies are absent.
UNINTERPRETABLE	An uninterpretable result means that a non-specific reaction occurred when testing the patient sample. See TP-PA results.

For questions or additional information, please contact Kristine Smith by email at smithk8@michigan.gov

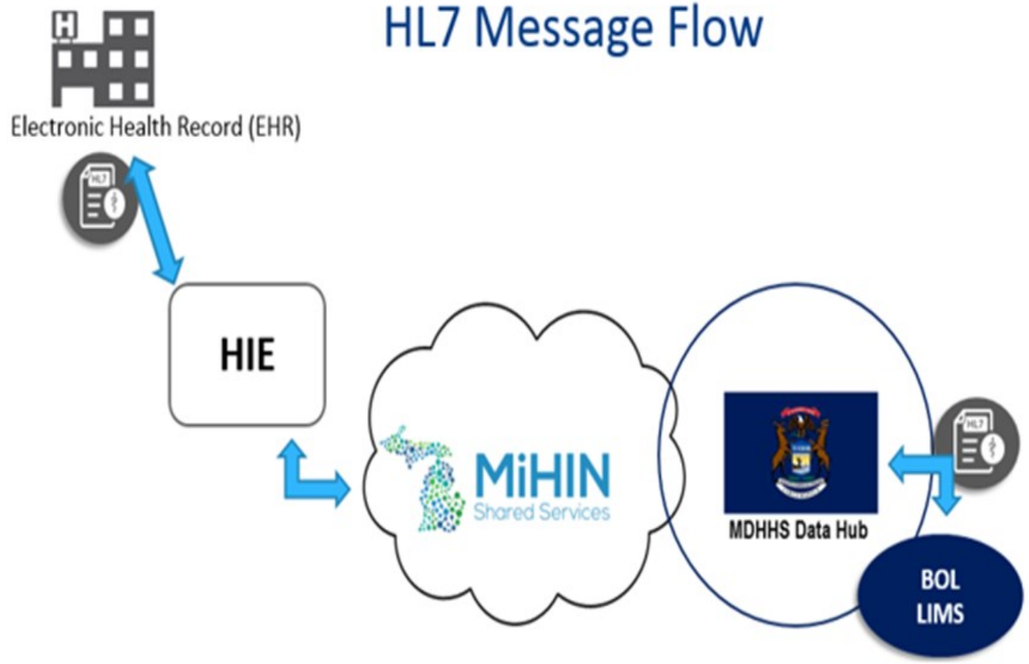
Bureau of Laboratories Needs Pilots

Author: Julie Kusey, Laboratory Systems Section Manager

The Michigan Department of Health and Human Services Bureau of Laboratories (MDHHS BOL) is seeking pilots for incoming and outgoing electronic HL7 messaging for test orders and results for most infectious disease testing performed at the State Public Health Laboratory. The receipt of orders and results in near real-time is expected to improve patient health and reduce health care costs through early detection and intervention. The development of electronic messages that can transmit an order and return test results to the ordering provider will significantly reduce the burden on providers by eliminating the need for hand-written forms and filing of patient results, reduce the risk for transcription errors by both parties, and decrease time for patient results to become available to the health care provider.

HL7 PROCESS MAP

Laboratory test orders are initiated in the provider's Electronic Health Record (EHR), routed through the provider's Health Information Exchange (HIE) network, to Michigan Health Information Network (MiHIN) for Electronic Service Information (ESI) lookup, to the Data Hub, and into the BOL laboratory information management system (LIMS). Completed laboratory test results are returned to the EHR through the same route.



The BOL is currently enrolling laboratories to pilot these projects. If your facility would like to participate in our pilot project, please contact Julie Kusey at kuseyj@michigan.gov or Paul Porras at paul.porras@mihin.org .

LabLink is published quarterly by the Michigan Department of Health and Human Services, Bureau of Laboratories, to provide laboratory information to Michigan health professionals and public health community.

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Editor: Teresa Miller , BAS, Laboratory Scientist